Effect of Ranibizumab Treatment in Cases of Choroidal Neovascular Membranes Secondary to Pathological Myopia versus Age-Related Macular Degeneration

Thesis

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بسم الله الرحمن الرحيم
وَأَنْزَلَ اللهُ عَلَيْكَ
الْكِتَابَ وَالْحِكْمَةَ
وَعَلَّمَكَ مَا لَمْ
تَكُنْ تَعْلَمُ وَكَانَ
فَضْلُ اللهِ عَلَيْكَ
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Mohammed Shaalan Abd Al-Tawab

List of Contents

List of Tables

Table No.	Title	Page No.

List of Figures

List of Figures cont...

List of Figures cont...

List of Abbreviations

Abb.	Full term
AEs	*Adverse events*
AMD	*Age-related macular degeneration*
AREDS	*Age-related eye disease study*
AT	*Average thickness*
BM	*Bruch's membrane*
CFT	*Central foveal thickness*
CME	*Cystoid macular edema*
CMT	*Central macular thickness*
CNV	*Choroidal neovascularization*
CNVM	*Choroidal neovascular membrane*
CRA	*Chorioretinal atrophy*
FAZ	*Foveal avascular zone*
FFA	*Fundus fluorescein angiography*
GA	*Geographic atrophy*
HRDs	*Hyper-reflective dots*
ICG	*Indocyanine green*
IOP	*Intraocular pressure*
MCNV	*Myopic choroidal neovascularization*
OCT	*Optical coherence tomography*
PCV	*Polypoidal choroidal vasculopathy*
PDT	*Photodynamic therapy*
PED	*Pigment epithelial detachment*
PEDF	*Pigment epithelial derived factor*
PlGF	*Placental growth factor*

List of Abbreviations cont...

Abb.	Full term
PRN	*Pro re nata*
RAP	*Retinal angiomatous proliferation*
RPE	*Retinal pigment epithelium*
SD-OCT	*Spectral Domain Optical Coherence Tomography*
SRF	*Subretinal fluid*
TV	*Total volume*
VA	*Visual acuity*
VEGF	*Vascular endothelial growth factor*
VEGFR	*Vascular endothelial growth factor receptor*
VMA	*Vitreomacular adhesion*

INTRODUCTION

Pathological myopia is a major cause of legal blindness in many developed and developing countries, It is associated with progressive elongation of the globe, which may be accompanied by degenerative changes in the sclera, choroid, Bruch's membrane, retinal pigment epithelium (RPE), and neurosensory retina. The most common vision-threatening complication of pathological myopia is the development of choroidal neovascularization (CNV) at the macula. In many countries, pathological myopia is the commonest cause of CNV in younger patients ***(Hampton et al., 1983).***

Age-related macular degeneration (AMD), also known as age-related maculopathy (ARM), is a degenerative disorder affecting the macula of elderly patients. It is characterized by the presence of specific clinical findings including drusen and retinal pigment epithelium (RPE) changes as early features with no evidence that the signs are secondary to another disorder. Later stages of the disease are associated with impairment of vision ***(Bowling, 2016).***

Conventionally AMD is divided into two main types:

- ***Dry (non-exudative) AMD*** is the most common form, comprising around 90% of diagnosed disease; geographic atrophy (GA) is the advanced stage of dry AMD ***(Bowling, 2016).***

- ***Wet (exudative) AMD*** is much less common than dry, but is associated with more rapid progression to advanced sight loss. The main manifestations are Choroidal neovascularization (CNV) and pigment epithelial detachment (PED). Occasionally, the dry form can develop into the wet form ***(Bowling, 2016).***

The disease virtually always begins as the non-neovascular or dry form of AMD and may progress to geographic atrophy or the neovascular (wet) form of the disease in one or both eyes. When neovascularization occurs, there is accumulation of fluid, hemorrhage, and lipid exudation within the macula that can culminate in fibrosis referred to as a disciform scar ***(Zarbin et al., 2004).***

AMD is the leading cause of irreversible visual impairment among the elderly worldwide affecting 30–50 million individuals ***(de Jong et al. 2006).*** The cause of AMD is multifactorial and influenced by age, ethnic background, and a combination of environmental and genetic factors ***(Zarbin, 2004).***

Up till now there is no effective medical treatment for AMD; however, vitamin supplementation, good nutrition, and cessation of smoking can slow the progression of the dry form of AMD ***(Bressler et al., 2003),*** while drugs that inhibit vascular endothelial growth factor-A (VEGF-A) have been successful in converting the wet form of AMD back to the dry form ***(Brown et al., 2006).***

CNV refers to the growth of neovasculature derived from the choroidal vessels through breaks in Bruch's membrane into the sub-retinal pigment epithelium or sub-retinal space. CNV is associated with a number of disorders, but the most important one is AMD ***(Bai et al., 2014).***

The principle test to diagnose CNV is fluorescein angiography (FFA). Spectral domain optical coherence tomography (SDOCT) is used to help guide clinical management of neovascular AMD patients by providing a cross-sectional view of the retinal depth, visualization of subretinal fluid (SRF), and quantitative measurement of central subfield thickness (CST) ***(Mohammad et al., 2014).***

Photocoagulation and photodynamic therapy (PTD), were the conventional lines of treatment of CNV until focus was directed to other causes that attribute to the formation of CNV particularly the effect of vascular endothelial growth factor (VEGF), which binds to endothelial cell receptors, promoting angiogenesis and vascular leakage ***(Bowling, 2016).***

Ranibizumab (Lucentis®, Novartis Pharma AG, Switzerland) is a recombinant, humanized, monoclonal antibody fragment designed to inhibit the active forms of vascular endothelial growth factor A (VEGF-A). VEGF-A is important in the pathogenesis of CNV, stimulating the growth of new blood vessels and increasing vascular leakage ***(Claxton et al., 2014).***

AIM OF THE WORK

The aim of this work is to compare the response of treatment with ranibizumab in cases of CNV secondary to pathological myopia versus CNV secondary to age-related macular degeneration by using OCT and FFA.

Chapter 1

ANATOMY AND PHYSIOLOGY OF THE RETINA

Anatomy of the retina

Layers of the retina

The retina consists of 10 layers, which are actually a remarkable organization of alternate groupings of the retinal neurons and their processes (Fig. 1):

1. Retinal pigment epithelium (RPE)
2. Photoreceptor cell layer
3. External limiting membrane
4. Outer nuclear layer (ONL)
5. Outer plexiform layer (OPL)
6. Inner nuclear layer (INL)
7. Inner plexiform layer (IPL)
8. Ganglion cell layer (GCL)
9. Nerve fiber layer (NFL)
10. Internal limiting membrane (ILM)

(VanPutte et al., 2014)